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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,832	05/03/2005	Jerry Leroy Adams	P51379	6108

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EXAMINER	
MABRY, JOHN	
ART UNIT	**PAPER NUMBER**
1625	

NOTIFICATION DATE	DELIVERY MODE
06/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/533,832	ADAMS ET AL.	
	Examiner	Art Unit	
	John Mabry, PhD	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/03/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification Objections

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The current title is "Chemical Compounds". Examiner suggests a title that directed towards Applicants' invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for salts, does not reasonably provide enablement for hydrates and solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are drawn to hydrates and solvates. But the numerous examples presented all failed to produce a hydrate or solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants should provide sufficient evidence that solvates can be made, or limit the claims accordingly.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "salts", does not reasonably provide enablement for "prodrugs". Based upon the Specification and art recognized terminology, the phrase "physiologically functional derivatives" is interpreted to be equivalent to the term "prodrug". Examiner interprets The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The nature of the invention in the instant case has claims which embrace aryl piperidine compounds. The scope of "prodrug" is not adequately enabled. Applicants provide no guidance as how the compounds are made more active *in vivo*. The choice of a "prodrug" will vary from drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrugs will be suitable for the instant invention.

The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would no how to prepare the various compounds suggested by said claims. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

n = 1 and 2

R^A = -CONHR1 wherein R1= H, phenyl, pyridinyl, piperidinyl, pyrrolinyl, morpholinyl, unsubstituted and substituted where substitution is –CO2R1a, -CONR1aR1b where R1a and R1b=H, alkyl, cycloalkyl, phenyl

R^B = -CONHR3, -SO2R3 wherein R3=H, alkyl, phenyl, thienyl, isoxazolyl, pyridinyl, pyrazolyl, morpholinyl, piperazinyl unsubstituted and substituted where substitution is alkyl amino, morpholinyl, pyrrolidinyl,

but does not reasonably provide enablement for:

n = 3

R^A =

R^A is -NHR^1, -$NHCOR^1$, -$NHCONHR^1$, -$NHCO_2R^1$, -$NHSO_2R^1$ or -$NHSO_2NHR^1$;

wherein R^1 is or an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl- or heteroaryl-C_1-C_4 alkyl- group,

where said optionally substituted R^1 group is optionally substituted with one or more substituents independently selected from halogen, -R^{1a}, -OR^{1a}, -SR^{1a}, -SO_2R^{1c} -$NR^{1a}R^{1b}$, cyano, nitro, -COR^{1c}, -$NR^{1b}COR^{1a}$, -$CONR^{1a}R^{1b}$, -$NR^{1b}SO_2R^{1c}$, and -$SO_2NR^{1a}R^{1b}$,

where R^{1a} is or an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

R^{1b} is unsubstituted C_1-C_4 alkyl, and

R^{1c} is an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-,

heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

where each optionally substituted R^{1a} group and R^{1c} group is independently optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, -OC_1-C_4 alkyl, -OC_1-C_4 haloalkyl, halogen, -OH, -NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), cyano, nitro, oxo, -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -OC(O)C_1-C_4 haloalkyl, -SO_2(C_1-C_4 alkyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -NHS(O)$_2$(C_1-C_4 alkyl), and -NHS(O)$_2$(C_1-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_4 alkyl,

or R^{1a} and R^{1c}, together with the nitrogen atom to which they are attached, form an optionally substituted heterocycyl or heteroaryl ring which optionally contains one or more additional heteroatom moieties selected from O, S, SO, SO_2, N and N→O, wherein said optionally substituted heterocycyl or heteroaryl ring is optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, -OC_1-C_4 alkyl, -OC_1-C_4 haloalkyl, halogen, -OH, -NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), cyano, nitro, oxo, -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -OC(O)C_1-C_4 haloalkyl, -SO_2(C_1-C_4 alkyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -NHS(O)$_2$(C_1-C_4 alkyl), and -NHS(O)$_2$(C_1-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_4 alkyl,

R^B =

R^B is -CO_2R^3, -COC(R^4R^5)R^5,

wherein R^3 is an optionally substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl- or heteroaryl-C_1-C_4 alkyl- group,

where said optionally substituted R^3 group is optionally substituted with one or more substituents independently selected from halogen, -R^{3a}, -OR^{3a}, -SR^{3a},

R2 =

wherein R^2 is hydrogen or an optionally substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl- or heteroaryl-C_1-C_4 alkyl- group,

where said optionally substituted R^2 group is optionally substituted with one or more substituents independently selected from halogen, $-R^{2a}$, $-OR^{2a}$, $-SR^{2a}$, $-SO_2R^{2c}$ $-NR^{2a}R^{2b}$, cyano, nitro, $-COR^{2c}$, $-CO_2R^{2a}$, $-NR^{2b}COR^{2a}$, $-CONR^{2a}R^{2b}$, $-NR^{2b}SO_2R^{2c}$, and $-SO_2NR^{2a}R^{2b}$,

where R^{2a} is hydrogen or an optionally substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-,

C_3-C_7 cycloalkyl-C_2-C_6 alkynyl-, heteroaryl-C_2-C_6 alkynyl-, or heterocycyl-C_2-C_6 alkynyl- group,

R^{2b} is hydrogen or unsubstituted C_1-C_6 alkyl, and

R^{2c} is an optionally substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

where each optionally substituted R^{2a} group and R^{2c} group is independently optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, -OC_1-C_4 alkyl, -OC_1-C_4 haloalkyl, halogen, -OH, -NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), cyano, nitro, oxo, -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -OC(O)C_1-C_4 haloalkyl, -SO_2(C_1-C_4 alkyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -NHS(O)$_2$(C_1-C_4 alkyl), and -NHS(O)$_2$(C_1-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_4 alkyl,

or R^{2a} and R^{2b}, together with the nitrogen atom to which they are attached, form an optionally substituted heterocycyl or heteroaryl ring which optionally contains one or more additional heteroatom moieties selected from O, S, SO, SO_2, N and N→O, wherein said optionally substituted heterocycyl or heteroaryl ring is optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, -OC_1-C_4 alkyl, -OC_1-C_4 haloalkyl, halogen, -OH, -NH_2, -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NH(C_1-C_4 alkyl), cyano, nitro, oxo, -CO_2H, -C(O)OC_1-C_4 alkyl, -CON(C_1-C_4 alkyl)(C_1-C_4 alkyl), -CONH(C_1-C_4 alkyl), -$CONH_2$, -NHC(O)(C_1-C_4 alkyl), -C(O)C_1-C_4 alkyl, -C(O)C_1-C_4 haloalkyl, -OC(O)C_1-C_4 alkyl, -OC(O)C_1-C_4 haloalkyl, -SO_2(C_1-C_4 alkyl), -SO_2(C_1-C_4 haloalkyl), -SO_2NH_2, -SO_2NH(C_1-C_4 alkyl), -NHS(O)$_2$(C_1-C_4 alkyl), and -NHS(O)$_2$(C_1-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_4 alkyl,

$-SO_2R^{3c}$ $-NR^{3a}R^{3b}$, $-COR^{3c}$, $-CO_2R^{3a}$, $-NR^{3b}COR^{3a}$, $-CONR^{3a}R^{3b}$, $-NR^{3b}SO_2R^{3c}$, and $-SO_2NR^{3a}R^{3b}$,

where R^{3a} is hydrogen or an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

R^{3b} is hydrogen or unsubstituted C_1-C_4 alkyl, and

R^{3c} is an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

where each optionally substituted R^{3a} group and R^{3c} group is independently optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, $-OC_1$-C_4 alkyl, $-OC_1$-C_4 haloalkyl, halogen, -OH, $-NH_2$, $-N(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-NH(C_1$-C_4 alkyl), cyano, nitro, oxo, $-CO_2H$, $-C(O)OC_1$-C_4 alkyl, $-CON(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-CONH(C_1$-C_4 alkyl), $-CONH_2$, $-NHC(O)(C_1$-C_4 alkyl), $-C(O)C_1$-C_4 alkyl, $-C(O)C_1$-C_4 haloalkyl, $-OC(O)C_1$-C_4 alkyl, $-OC(O)C_1$-C_4 haloalkyl, $-SO_2(C_1$-C_4 alkyl), $-SO_2(C_1$-C_4 haloalkyl), $-SO_2NH_2$, $-SO_2NH(C_1$-C_4 alkyl), $-NHS(O)_2(C_1$-C_4 alkyl), and $-NHS(O)_2(C_1$-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_8 alkyl,

or R^{3a} and R^{3b}, together with the nitrogen atom to which they are attached, form an optionally substituted heterocycyl or heteroaryl ring which optionally contains one or more additional heteroatom moieties selected from O, S, SO, SO_2, N and N→O, wherein said optionally substituted heterocycyl or heteroaryl ring is optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, $-OC_1$-C_4 alkyl, $-OC_1$-C_4 haloalkyl, halogen, -OH, $-NH_2$, $-N(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-NH(C_1$-C_4 alkyl), cyano, nitro, oxo, $-CO_2H$, $-C(O)OC_1$-C_4 alkyl, $-CON(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-CONH(C_1$-C_4 alkyl), $-CONH_2$, $-NHC(O)(C_1$-C_4 alkyl), $-C(O)C_1$-C_4 alkyl, $-C(O)C_1$-C_4 haloalkyl, $-OC(O)C_1$-C_4 alkyl, $-OC(O)C_1$-C_4 haloalkyl, $-SO_2(C_1$-C_4 alkyl), $-SO_2(C_1$-C_4 haloalkyl), $-SO_2NH_2$, -

$-SO_2R^{3c}$ $-NR^{3a}R^{3b}$, $-COR^{3c}$, $-CO_2R^{3a}$, $-NR^{3b}COR^{3a}$, $-CONR^{3a}R^{3b}$, $-NR^{3b}SO_2R^{3c}$, and $-SO_2NR^{3a}R^{3b}$,

where R^{3a} is hydrogen or an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

R^{3b} is hydrogen or unsubstituted C_1-C_4 alkyl, and

R^{3c} is an optionally substituted C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, aryl, C_3-C_7 cycloalkyl, heteroaryl, heterocyclyl, aryl-C_1-C_4 alkyl-, C_3-C_7 cycloalkyl-C_1-C_4 alkyl-, heteroaryl-C_1-C_4 alkyl-, heterocycyl-C_1-C_4 alkyl-, aryl-C_2-C_4 alkenyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkenyl-, heteroaryl-C_2-C_4 alkenyl-, heterocycyl-C_2-C_4 alkenyl-, aryl-C_2-C_4 alkynyl-, C_3-C_7 cycloalkyl-C_2-C_4 alkynyl-, heteroaryl-C_2-C_4 alkynyl-, or heterocycyl-C_2-C_4 alkynyl- group,

where each optionally substituted R^{3a} group and R^{3c} group is independently optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, $-OC_1$-C_4 alkyl, $-OC_1$-C_4 haloalkyl, halogen, -OH, $-NH_2$, $-N(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-NH(C_1$-C_4 alkyl), cyano, nitro, oxo, $-CO_2H$, $-C(O)OC_1$-C_4 alkyl, $-CON(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-CONH(C_1$-C_4 alkyl), $-CONH_2$, $-NHC(O)(C_1$-C_4 alkyl), $-C(O)C_1$-C_4 alkyl, $-C(O)C_1$-C_4 haloalkyl, $-OC(O)C_1$-C_4 alkyl, $-OC(O)C_1$-C_4 haloalkyl, $-SO_2(C_1$-C_4 alkyl), $-SO_2(C_1$-C_4 haloalkyl), $-SO_2NH_2$, $-SO_2NH(C_1$-C_4 alkyl), $-NHS(O)_2(C_1$-C_4 alkyl), and $-NHS(O)_2(C_1$-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_8 alkyl,

or R^{3a} and R^{3b}, together with the nitrogen atom to which they are attached, form an optionally substituted heterocycyl or heteroaryl ring which optionally contains one or more additional heteroatom moieties selected from O, S, SO, SO_2, N and N→O, wherein said optionally substituted heterocycyl or heteroaryl ring is optionally substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, $-OC_1$-C_4 alkyl, $-OC_1$-C_4 haloalkyl, halogen, -OH, $-NH_2$, $-N(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-NH(C_1$-C_4 alkyl), cyano, nitro, oxo, $-CO_2H$, $-C(O)OC_1$-C_4 alkyl, $-CON(C_1$-C_4 alkyl$)(C_1$-C_4 alkyl), $-CONH(C_1$-C_4 alkyl), $-CONH_2$, $-NHC(O)(C_1$-C_4 alkyl), $-C(O)C_1$-C_4 alkyl, $-C(O)C_1$-C_4 haloalkyl, $-OC(O)C_1$-C_4 alkyl, $-OC(O)C_1$-C_4 haloalkyl, $-SO_2(C_1$-C_4 alkyl), $-SO_2(C_1$-C_4 haloalkyl), $-SO_2NH_2$, -

$SO_2NH(C_1$-C_4 alkyl), -$NHS(O)_2(C_1$-C_4 alkyl), and -$NHS(O)_2(C_1$-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_4 alkyl, and

R^4 and R^5 are independently selected from hydrogen and unsubstituted C_1-C_4 alkyl,

or R^4 and R^5, taken together with the carbon atom to which they are attached, represent an optionally substituted 3-6-membered saturated carbocyclic ring, where said optionally substituted 3-6-membered ring is substituted with one or more substituents independently selected from C_1-C_4 alkyl, C_1-C_4 haloalkyl, -OC_1-C_4 alkyl, -OC_1-C_4 haloalkyl, halogen, -OH, -NH_2, -$N(C_1$-C_4 alkyl)(C_1-C_4 alkyl), -$NH(C_1$-C_4 alkyl), cyano, nitro, oxo, -CO_2H, -$C(O)OC_1$-C_4 alkyl, -$CON(C_1$-C_4 alkyl)(C_1-C_4 alkyl), -$CONH(C_1$-C_4 alkyl), -$CONH_2$, -$NHC(O)(C_1$-C_4 alkyl), -$C(O)C_1$-C_4 alkyl, -$C(O)C_1$-C_4 haloalkyl, -$OC(O)C_1$-C_4 alkyl, -$OC(O)C_1$-C_4 haloalkyl, -$SO_2(C_1$-C_4 alkyl), -$SO_2(C_1$-C_4 haloalkyl), -SO_2NH_2, -$SO_2NH(C_1$-C_4 alkyl), -$NHS(O)_2(C_1$-C_4 alkyl), and -$NHS(O)_2(C_1$-C_4 haloalkyl), where said C_1-C_4 alkyl is unsubstituted C_1-C_4 alkyl.,

or a salt, solvate, or physiologically functional derivative thereof.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The Specification does not provide any support for said variables at n, R^A, R^B and R2 positions. Pages 31-33 (Schemes 1 and 2) of the Specification describe starting materials and methods for synthesis of compounds wherein n, R^A, R^B and R2 as mentioned above, but does not describe or list any reagents wherein compounds can be used to synthesis compounds where n, R^A, R^B and R2 as listed above.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.

1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims: Scope of the compounds. Owing to the range of many variables, millions of highly substituted indolinyl and 1,2,3,4-tetrahydroquinolinyl compounds are embraced.

(2) The nature of the invention: The invention is a highly substituted indolinyl and 1,2,3,4-tetrahydroquinolinyl compounds.

(3) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and chemical reactivity (which is affected by determinants such as substituent effects, steric effects, bonding, molecular geometry, etc) is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(4) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of compounds of application's general formula I. Pages 31-33 (Schemes 1 and 2) of the Specification describes starting materials and methods for synthesis of compounds wherein n, R^A, R^B and R2 as aforementioned, but does not describe or list any reagents wherein compounds can be used to synthesis compounds where n, R^A, R^B and R2 as listed above. There is limited evidence in the Specification of the example compounds that only covers no or a small portion of the substituents claimed of formula I. Thus, there is no specific direction or guidance regarding said compounds specifically mentioned in Scope.

The availability of the starting material that is needed to prepare the invention as claimed is at issue here…As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court *in re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691

(CCPA 1981).

Additionally, the Applicant is not enabled for all aryl, heteroaryl, heterocyclyl, optional substituents, substitution patterns and functional groups as claimed and described in Specification on pages 10-12.

(5) State of the Prior Art: These compounds are substituted indolinyl and 1,2,3,4-tetrahydroquinolinyl compounds wherein n, R^A, R^B and R2. So far as the examiner is aware, no substituted indolinyl and 1,2,3,4-tetrahydroquinolinyl compounds of general formula I wherein n, R^A, R^B and R2 as listed above of any kind have been made or used.

It is not trivial to experimentally interchange any and all of the many substituents that exist. As described by F. Zaragoza Dörwald, most organic syntheses fail initially and chemical research is highly inefficient due to chemists spending most of their time "finding out what went wrong and why". Therefore, most syntheses of organic compounds are labor-intensive and demanding. Additionally, most final synthetic routes to desired organic molecules are usually very different from initially planned routes. A highly skilled chemist can agree that for many successful organic compounds made, many failures are encountered and experimental repetition is common. This also contributes to the burden and unpredictability of the syntheses of said compounds. (see "Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design" 2005

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(6) Working Examples: Applicant shows examples 1-103 (pages 35-62) but no working examples were shown wherein n, R^A, R^B and R2 (and other variables therein) equal aforementioned substituents have been made or used of any kind.

(7) Skill of those in the art: The ordinary artisan is highly skilled, e.g. a masters or PhD level chemist.

(8) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for inhibition of TIE-2 kinase, VEGFR-2 and -3 and Raf kinase with undisclosed species of Formula I in an assay; the Application is not

enabled for treatment treating related diseases and altering related physiological functions and disorders in a mammal more specifically treating cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims: Treatment of all claimed diseases and disorderes related to TIE-2 kinase, VEGFR-2 and -3 and Raf kinase comprising the step of administering to a mammal using substituted biaryl-carboxylate compounds of Formula I.

(2) The nature of the invention: The invention is the method of using substituted indolinyl and 1,2,3,4-tetrahydroquinolinyl compounds of Formula I to treat related diseases and altering related physiological functions and disorders in a mammal more specifically treating cancer comprising the step of administering to a mammal.

(3) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and

physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(4) Direction or Guidance: While being enabled for inhibition of TIE-2 kinase, VEGFR-2 and -3 and Raf kinase with undisclosed species of Formula I in an assay; the Application is not enabled for treatment treating related diseases and altering related physiological functions and disorders in a mammal more specifically treating cancer. The Applicant does not show or demonstrate the use compounds and compositions of Formula I towards all claimed treatment of diseases and disorders and altering related physiological functions and disorders as claimed.

The Specification assays of TIE-2 kinase, VEGFR-2 and -3 and Raf kinase with undisclosed species of Formula I and describes the process of how to executed said assay, but shows no biological data pertaining to the outcome of these assays. The Specification only discloses the IC50 values of undisclosed species of Formula I that pertains to each mention assay. Additionally, the Applicant does not specifically disclose the exact compounds that were administered during these *in vitro* studies. The only information provided pertaining to the compounds tested is on page 17, line 32, which vaguely describes, "test compounds". However, there is very limited guidance or direction as how to treat related diseases and altering related physiological functions and disorders in a mammal more specifically treating cancer. using compounds of Formula I.

(5) State of the Prior Art: Treatment of related diseases and disorder and altering related physiological functions and disorders in a mammal more specifically treating cancer is not well developed and is highly unpredictable. The state of the prior art for their treatments involve screening, *in vitro* and *in vivo,* that provides data to determine if compounds exhibit the desired physiological altering functions and affect on its related diseases and disorders as claimed. The Applicant has not provided any art recognized evidence that shows the use of compounds and compositions claimed for the claimed uses.

The state of the prior art is not well developed and is highly unpredictable. According to the Specification, Applicant's compounds (as listed above) are alleged to exhibit inhibitory activity. However, the Specification does not set forth any the *in vitro* assays. There are no teachings of how to use the claimed compounds *in vivo.* There is insufficient disclosure to reasonably predict that the methods and compositions of the instant Specification would treat related diseases and disorder and altering related physiological functions and disorders in a mammal more specifically treating cancer using claimed compounds *in vitro* or *in vivo.* This is merely an unsubstantiated assertion with no evidence to support the contention that election species would inhibit TIE-2 kinase, VEGFR-2 and -3 and Raf kinase with undisclosed species of Formula I. Applicant has not shown any cell culture data or *in vivo* studies for treating affected mammals. The Applicant has not shown any art recognized correlation between the data shown and the scope of the claimed invention.

Even in the event the Applicant did provide *in vivo* and *in vitro* studies, the ordinary artisan would recognize and appreciate that there is no known correlation between *in vitro* and *in vivo* results, because the artisan recognizes that an *in vitro* assay cannot duplicate the complex conditions of in vivo therapy. In the in vitro assay, the agent is in contact with cells during the entire exposure period. This is not the case in vivo where exposure to the target site may be delayed or inadequate. In addition, variables such as biological stability, half-life, or clearance from the blood are important parameters in achieving successful therapy. The composition may be inactivated *in vivo* before producing a sufficient effect, for example, by proteolytic degradation or immunological activation. In addition, the composition may not reach the target cells because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by fluids, cells, and tissues where the composition has no effect and/or a large enough local concentration may not be established. There are no specific teachings in the disclosure that would allow one to have a reasonable expectation of success in transferring the in vitro method to treat affected patients. One is only left with speculation and an invitation to experiment. Given the breadth of the claims which encompass treatment and the lack of examples and guidance as discussed above, one of ordinary skill in the art would reasonably have considered that at the time the application was filed, that the Applicant was not in possession of the claimed invention.

(6) Working Examples: The Applicant has provided no working examples. Nor has Applicant directed the skilled artisan to disclosures in the art that may be used to

extrapolate the intended use of the compounds and compositions for demonstrate the use compounds and compositions of Formula I towards all claimed treatment of diseases and disorders and altering related physiological functions and disorders as claimed.

(7) Skill of those in the art: The ordinary artisan is highly skilled such as a medical doctor, doctor of philosophy in science, a nurse practitioner, etc.

(8) The quantity of experimentation needed: In the absence of working examples, which provide sufficient representative disclosures necessary to provide enablement for the treatment and prevention of pain and inflammation, undue experimentation would indeed be required to practice the instant invention. The amount of experimentation is expected to be unduly high and burdensome.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

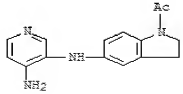
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Effland et al (US 4,970,219) (PTO-1449) in view of Majno (American J. Pathology 1998, 153, 1035-1039).

The instant application claims compounds and pharmaceutical compositions of Formula I wherein n=1, R^B=-COCH3, X=NH and R^A=NH2.

Scope & Content of Prior Art MPEP 2141.01

Effland discloses compounds and pharmaceutical compositions of Formula I wherein n=1, R^B=-COCH3, X=NH and R^A=NH2 (see column 7, line 43).



Differences between Prior Art & the Claims MPEP 2141.02

The instant application differs from Effland at positions of a) R^A and b) X which both are considered positional isomers - a) Applicant's R^A bonded to carbon adjacent to N on pyridine ring versus Efflands R^A being two carbons removed from N on pyridine ring and b) Applicant's -NH being being at *ortho* position (4-position) versus Effland's –NH being at *meta* position (3-position).

However, Effland teaches that both of said substituents can be positioned at any position of pyridinyl ring of Formula I (see column 1).

Additionally, there is little difference between a) Applicant's R^A bonded to carbon adjacent to N on pyridine ring versus Efflands RA being two carbons removed from N on pyridine ring and b) Applicant's -NH being being at *ortho* position (4-position) versus Effland's –NH being at *meta* position (3-position) of formula I. It is well established that position isomers are prima facie structurally obvious even in the absence of a teaching to modify. The isomer is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the position isomers. This circumstance has arisen many times. See: *Ex parte Englehardt,* 208 USPQ 343, 349; *In re Mehta,* 146 USPQ 284, 287; *In re Surrey*, 138 USPQ 67; *Ex Parte Ullyot,* 103 USPQ 185; *In re Norris,* 84 USPQ 459; *Ex. Parte Naito,* 168 USPQ 437, 439; *Ex parte Allais,* 152 USPQ 66; *In re Wilder*, 166 USPQ 545, 548; *Ex parte Henkel,* 130 USPQ 474; *Ex parte Biel,* 124 USPQ 109; *In re Petrzilka,* 165 USPQ 327; *In re Crownse,* 150 USPQ 554; *In re Fouche,* 169 USPQ 431; *Ex parte Ruddy,* 121 USPQ 427; *In re Wiechert,* 152 USPQ 249, *In re Shetty,* 195 USPQ 753; *In*

re Jones, 74 USPQ 152, 154. There may be others as well. Thus, said claims are rendered obvious by Effland et al.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (*Englehardt*) and "Position isomerism is fact of close structural similarity" (*Mehta*, emphasis in the original). Note also *In re Jones,* 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to prima facie obviousness"; one of those listed is "adjacent homologues and structural isomers". Position isomers are the basic form of close "structural isomers." Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds…a known compound may suggest it analog or isomers, either geometric (cis v. trans) or position isomers (e.g. *ortho v. para*)." See also MPEP 2144.09, second paragraph. Further, the reference provides for the ring being substituted in any position.

Furthermore, the genus of Effland teaches R^A can be H, lower alkyl, aryl lower alkyl, or loweralkyl carbonyl (see column 1, lines 23-24), X=O and NR2 wherein R2 being H, lower alkyl or lower alkylcarbonyl (see column 1, lines 21-22) and R^B=H, lower alkyl carbonyl(see column 1, lines 62-63). Thus said, claims are rendered obvious over Effland.

Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413

It would be obvious to an artisan of ordinary skill to use the reference of Effland to achieve the invention of the instant application. One of ordinary skill would be motivated to use the species and teachings of Effland in order to inhibit TIE-2 kinase, VEGFR-2 and -3 and Raf kinase. Applicant claims that said enzymes are directly related to inhibiting growth factor receptor function which is directly linked to angiogenesis.

The reference of Effland discloses compounds of Formula I in order to treat inflammation. The instant application discloses compounds used to inhibit aforementioned enzymes to in order to control angiogenesis. Majno discloses a correlation between inflammation and angiogenesis (see introduction and entire disclosure). Therefore, it would be obvious to one of ordinary skill at the time the invention was made to use the reference of Effland to make and use claimed compounds of Formula I in order to inhibit said enzymes to treat related diseases.

The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in KSR noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Court quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006), stated that "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with

some rational underpinning to support the legal conclusion of obviousness.'" KSR, 550 U.S. at___, 82 USPQ2d at 1396. Exemplary rationales that may support a conclusion of obviousness include:

(A) Combining prior art elements according to known methods to yield predictable results;

(B) Simple substitution of one known element for another to obtain predictable results;

(C) Use of known technique to improve similar devices (methods, or products) in the same way;

(D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;

(E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. See MPEP § 214 3 for a discussion of the rationales listed above along with examples illustrating how the cited rationales may be used to support a finding of obviousness. See also

MPEP § 2144- §2144.09 for additional guidance regarding support for obviousness determinations.

The aforementioned reasons above describe rationales that support a conclusion of obviousness based upon the KSR International Co. v.Teleflex Inc. decision. At least letters (A), (C), (F) and (G) rationale is supported above.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, PhD, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry, PhD/
Examiner
Art Unit 1625

/Rita J. Desai/
Primary Examiner, Art Unit 1625